Amendments to the Drawings:

The attached sheets of drawings include changes to Fig. 1, Fig. 2, and Fig. 8. These sheets replace the original sheets corresponding to Fig. 1, Fig. 2, and Fig. 8. Previously omitted sequence identification numbers have been added.

Attachments:

Replacement sheets for Fig. 1, Fig. 2, and Fig. 8

Annotated Sheets Showing Changes

Remarks/Arguments

Information Disclosure Statement

References cited within the text of the specification were not intended to be considered as citing information that was material to patentability of the present invention, but rather were included as citations referencing the source of information, particularly where illustrations were provided regarding the various uses of the invention. As the examiner noted, applicants filed a proper information disclosure statement in October 2004.

Specification

The disclosure has been objected to because the application contains sequence disclosures in the figures (Figs. 1, 2, and 8) that have not corresponding sequence identifier. Replacement figures accompany this response, as does a new sequence listing, incorporating the sequences listed as 1 (SEQ ID NO: 13), 2 (SEQ ID NO: 14), and 4 (SEQ ID NO: 15) of Fig. 1, as well as the Tirt ORF with additional base pairs 5' and 3'(SEQ ID NO: 16), as shown in Fig. 2, and the polynucleotide (SEQ ID NO: 17) and amino acid (SEQ ID NO: 18) sequences of the Tirt plasmid (pTirt#16) construct at the plasmid/protein junction.

Claim Objections

Claims 1-7 have been objected to because claim 1 recites "an" group. Claim 1, as presently amended, recites "a" group.

Claim Rejections – 35 USC §112

Claims 1-4 and 10-14 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite. The examiner has asserted that the term "group II intron-type reverse transcriptase" is unclear and confusing. Applicants respectfully traverse the examiner's

rejection, as this is a term of art, and to those of skill in the art it describes a type of reverse transcriptase that is derived from a group II intron. In support of this assertion, applicants provide five references that use the term as a term of art and explain the meaning of the term (*i.e.*, Ng, B., *et al.*, "Reverse transcriptases: intron-encoded proteins found in thermophilic bacteria," Gene (2007) 393: 137-144; Lampson, B., "Prokaryotic reverse transcriptases," in Industrial Enzymes, Polaine, J. and McCabe, A.P. (eds.), ©2007 (Springer, Netherlands),p. 403-420; Chee, G.J. and Takami, H., "Housekeeping recA gene interrupted by group II intron in the thermophilic *Geobacillus kaustophilus*," Gene (2005) 363: 211-20; Michel, F. and Ferat, J., "Structure and activities of Group II introns," Ann. Rev. Biochem. (1995) 64: 435-61; Mohr, G., et al., "Evolutionary relationships among group II intron-encoded proteins and identification of a conserved domain that may be related to maturase function," Nuc. Acids Res. (1993) 21: 4991-4997). Applicants believe that use of the term is, and was, as of the date of filing of the application, widespread enough among those of skill in the art that there is no doubt as to what the term is intended to describe and define. Applicants distinguished the group II intron-derived sequence from a retron-derived sequence, for example, at page 8, lines 19-28 (paragraph 20).

Claims 1-4 and 10-14 have been rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the invention at the time the application was filed and as not providing enablement for polypeptide variants having at least 80% sequence identity with SEQ ID NO: 2. Applicants respectfully traverse this rejection, as they demonstrated in the specification (see page 9, lines 10-28

(paragraph 20)) and in the drawings (see Fig. 1) that there is significant variability between the reverse transcriptases derived from various bacteria, yet they retain their RT activity. Given the information provided, it is clear to someone of skill in the art that amino acid substitutions may be made in particular regions of the protein without affecting its RT activity. Furthermore, given the availability of gene-synthesis and peptide/protein-synthesis services and the fact that all the reagents needed to test the catalytic activity of any mutant made by modifying the sequence are readily available in a variety of commercial kits, while it might take additional funds to identify catalytically-active mutants, it would not take undue effort.

Among the Wands factors is the consideration as to the amount of guidance presented, the nature of the invention, the relative skill of those in the art, and the predictability or unpredictability of the art. In the present situation, the inventors have identified a specific sequence that encodes a group II intron reverse transcriptase, and have demonstrated that it shares certain sequence similarities with other bacterial RTs. They have also demonstrated that there is considerably genetic and peptide variability that is tolerated in the sequences of the RTs. Those of skill in the art are individuals with expertise in recombinant DNA techniques and expertise in designing proteins based on existing sequences. These individuals have at their fingertips the means to rapidly incorporate mutations into proteins and to rapidly test the effects of those mutations, where the catalytic effect of the protein may be examined in a test tube with a limited number of standard reagents. Applicants respectfully submit that both the written description and the enablement requirements have therefore been met by the present disclosure and that it is commensurate with the breadth of the claims.

According to MPEP section 2164.01(a), in Wands,

> "[t]he Court held that the specification was enabling with respect to the claims at issue and found that 'there was considerable direction and guidance' in the specification; there was 'a high level of skill in the art at the time the application was filed;' and 'all of the methods needed to practice the invention were well known.' 858 F.2d at 740, 8 USPQ2d at 1406. After considering all the factors related to the enablement issue, the court concluded that 'it would not require undue experimentation to obtain antibodies needed to practice the claimed invention.' *Id.*, 8 USPQ2d at 1407."

Applicants submit that modifying a protein that has been described by those who isolated it, especially when sequence comparisons are available between that protein and other proteins which serve similar functions, and assaying that protein's activity, especially when it acts as a polymerase (an activity that can be determined without the need for tissue culture or whole animal models) is certainly no more difficult for one of skill in the art of recombinant DNA technology than is the generation and isolation of specific types of antibodies.

Claim Rejections – 35 USC §102

Claim 1 has been rejected under 35 U.S.C. 102(e) as being anticipated by Gu *et al.* (U.S. Patent No. 7,094,539), under the assumption that Gu teaches the use of a reverse transcriptase. Applicants respectfully traverse this rejection. As previously stated, "group II intron-type reverse transcriptase" is a term of art known to those of skill in the art—the field of RNA and DNA polymerases. Gu *et al.* teach a composition comprising a DNA polymerase that has reverse transcriptase activity (see column 2, lines 7-9). Among the differences between the composition of Gu and the composition of the present invention are the lack of a maturase region ("X" domain) in the DNA polymerase described by Gu and the fact that there are proteins that are known as DNA polymerases, because their primary catalytic activity is to catalyze the formation of a DNA strand from a DNA template, and there are RNA polymerases,

whose primary catalytic activity is to catalyze the formation of a DNA strand from an RNA template. Some DNA polymerases may, under certain reaction conditions, also provide a reverse-transcriptase activity—but they are still categorized as DNA polymerases because this is their primary function. Gu describes a DNA polymerase. The present invention describes an RNA polymerase.

Respectfully submitted,

Donna Russell

Donna Russell, Ph.D., J.D.
Attorney for Applicants
Registration No. 46,252
Customer No. 41546